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APPLICATION FOR UNITED STATES LETTERS PATENT

for

GINSENG BERRY EXTRACTS AND PHARMACEUTICAL

COMPOSITIONS FROM GINSENG BERRY FOR THE

TREATMENT OF TYPE 2 DIABETES AND OBESITY

by

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BACKGROUND OF THE INVENTION

This application claims priority to U.S. Provisional Application No. 60/246,628, filed November 7, 2000.

The government owns rights in the present invention pursuant to grant number DK31842 from the National Institutes of Health, grant number DK44840 from the National Institutes of Health and grant number P60DK2059 from the National Institutes of Health.

I. Field of the Invention

The present invention relates generally to the fields of physiology and medicine. More particularly, it relates to pharmaceutical compositions and the methods of screening for constituents that are anti-hyperglycemic or anti-obesity agents. Such constituents can be extracted from ginseng berry.

II. Description of the Related Art

A. Diabetes mellitus

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Diabetes mellitus is a major health problem, affecting approximately 5% of the total population in the U.S., and 3% of the population world-wide. Diabetes mellitus is a chronic metabolic disease that can cause blindness, kidney failure, or nerve damage. In addition, diabetes mellitus confers an increased risk of ischemic heart disease, stroke and peripheral vascular disease. Over 90% of diabetics are classified as type 2, or non-insulin-dependent diabetes mellitus (NIDDM); the rest fall into the category of type 1, or insulin-dependent diabetes mellitus (IDDM). Although the two types of diabetes have distinct pathogeneses, hyperglycemia and various life-threatening complications resulting from long-term hyperglycemia are the most common features.

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1. Hyperglycemia in type 2 diabetes

Type 2 diabetes is characterized by fasting and post-prandial hyperglycemia. The fasting hyperglycemia is primarily caused by hepatic overproduction of glucose (Ferrannini *et al.*, 1989; Kruszynska and Olefsky, 1996). Impaired suppression of hepatic glucose production, together with impaired glucose uptake by insulin-target tissues such as skeletal muscle is responsible for postprandial hyperglycemia (Firth *et al.*, 1986; Mitrakou *et al.*, 1990; Kruszynska and Olefsky, 1996). Chronic hyperglycemia is not only a marker of diabetes, but is also a factor which itself worsens metabolic control. By inhibiting both insulin secretion and glucose utilization, chronic hyperglycemia self-perpetuates the diabetic state (Yki-Jarvinen, 1992). Moreover, prolonged exposure to hyperglycemia causes production of oxygen free radicals which may lead to β-cell defects (Brownlee *et al.*, 1984; Sakurai and Tsuchiya, 1988; Ihara *et al.*, 1999).

Clinicians have suspected for many years that the complications of diabetes are secondary to chronic hyperglycemia. Now, a large body of data from epidemiological studies (Liu et al., 1993; Klein et al., 1994; Stolk et al., 1995) and clinical trials (Abraira et al., 1995; Ohkubo et al., 1995) strongly support the conclusion that hyperglycemia is the principal cause of retinopathy, nephropathy, neuropathy, and cardiovascular complications. These complications constitute the major clinical and economical burden of diabetes. Diabetic complications also significantly contribute to decreased quality of life. Available evidence indicates that sustained reductions in hyperglycemia will decrease the risk of developing microvascular complications, and most likely reduce the risk of macrovascular complications (Gaster and Hirsch, 1998). Despite evidence for the benefits of improved glycemic control, a large percentage of people with type 2 diabetes maintain poor glucose control, in part, because of the limitations of therapies for the management of diabetes (Klein and Klein, 1998).

2. *Insulin resistance in type 2 diabetes*

One of the most important effects of insulin, with respect to type 2 diabetes, is the ability to stimulate glucose transport into tissues. Insulin-stimulated *in vivo* glucose